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Classic hairy cell leukemia with an aggressive presentation

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ABSTRACT

Hairy cell leukemia is an indolent neoplasm involving mature B cells with distinct cytologic and immunophenotypic features. It typically presents in older adults with pancytopenia and splenomegaly. We describe a patient who presented with severe anemia and thrombocytopenia, leukocytosis, and splenomegaly. He had an unusually complicated clinical course including pancytopenia refractory to multiple transfusions, oropharyngeal bleeding requiring intubation for airway protection, subdural hematoma after minor trauma, and sepsis due to *Staphylococcus aureus* bacteremia. This case highlights the importance of considering hairy cell leukemia in the differential diagnosis of all patients with cytopenia and splenomegaly, as this is a disease that has excellent response to treatment with purine analogs.

KEYWORDS Cladribine; hairy cell leukemia; leukocytosis; rituximab; splenomegaly

Hairy cell leukemia (HCL) is a rare chronic B cell lymphoproliferative neoplasm that was first described in 1956.[1,2] Common features of HCL include pan- or monocytopenia, splenomegaly without lymphadenopathy, and circulating "hairy" cells. The "hairy" cells are mature, neoplastic B cells with abundant cytoplasm showing characteristic hair-like projections. In the US, the estimated incidence is three cases per million per year; however, the prevalence is predicted to be much higher due to its indolent course. The median age at onset is 55 years, with a strong male predominance.[3] This case describes a unique presentation of a young patient with HCL and an unusually aggressive clinical course.

CASE DESCRIPTION

A 44-year-old white man presented to the emergency department after becoming dizzy and falling to the ground without loss of consciousness or head trauma. He had been feeling fatigued for a few months and developed bleeding gums, epistaxis, and a sore throat over the past week. On presentation, he was afebrile and hemodynamically stable. Initial laboratory results are shown in *Table 1*. Imaging revealed a subdural hematoma with midline shift, diffuse swelling of the brain, massive splenomegaly, and diffuse lymphadenopathy. He required intubation for airway protection due to oropharyngeal bleeding. Transfusion of packed red blood cells was started, and he was admitted to the medical intensive care unit.

The peripheral smear is shown in *Figure 1a*. Flow cytometry revealed a lambda light chain–restricted B cell population with an immunophenotype concerning for HCL *(Figure 2)*. Peripheral blood was tested for *BRAF* p.V600E by polymerase chain reaction, which was detected at 45.7%. He became febrile and was found to have methicillin-sensitive *Staphylococcus aureus* (MSSA) bacteremia, which was treated with antibiotics. His condition improved and he was extubated but continued to require multiple units of red blood cells, platelets, and fresh frozen plasma. Bone marrow biopsy and aspirate findings are described in *Figure 1b–1d*. The bone marrow was also positive for the *BRAF* p.V600E mutation. Peripheral blood and bone marrow morphology, together with the immunophenotype of the neoplastic B cells and the presence of the *BRAF* mutation, confirmed the diagnosis of HCL.

The patient was started on rituximab with a plan to delay initiation of cladribine until completion of the antibiotics for MSSA bacteremia. However, he remained transfusion dependent and developed hematuria and epistaxis, so he was readmitted and cladribine was initiated. He had a good

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Table 1. Initial laboratory values

Variable	Value (reference)
White blood cells (K/μL)	25 (3.6–9.5)
Red blood cells (M/μL)	0.91 (4.5–5.7)
Hemoglobin (g/dL)	3.0 (12–15)
Hematocrit (%)	10.2 (40–50)
Mean corpuscular volume (fL)	112.1 (80–100)
Platelets (K/μL)	31 (150–450)
Absolute neutrophil count (K/μL)	0.3 (1.4–6.0)
Neutrophils, manual absolute (K/μL)	1.0 (1.4–6.0)
Lymphocytes, manual absolute (K/μL)	23.6 (1.2–3.4)
Monocytes, manual absolute (K/μL)	0.8 (0.2–1.0)
Eosinophils, manual absolute (K/μL)	0.0 (0.0–0.5)
Basophils, manual absolute (K/μL)	0.0 (0.0–0.1)
Prothrombin time (sec)	16.1 (10.2–12.9)
International normalized ratio	1.4 (0.9–1.1)
Activated partial thromboplastin time (sec)	23.9 (25.1–36.5)
Reticulocyte count (%)	3.91 (0.5–2.0)
Haptoglobin (mg/dL)	367 (30–200)
Lactate dehydrogenase (IU/L)	138 (100–248)
Total bilirubin (mg/dL)	0.7 (0.2–1.2)

response to the first cycle of treatment, with improvement of anemia and thrombocytopenia to the point that he no longer required transfusions, but he remained neutropenic. He was continued on weekly rituximab for 4 weeks after completion of the cladribine, as it has been shown to improve complete response rates in HCL.[4] After the fourth cycle of rituximab, his hemoglobin improved to >11 g/dL, platelets to >100,000/mcL, and absolute neutrophil count to >1500/mcL, indicating a complete response.[5]

DISCUSSION

The patient in this case was relatively young to develop HCL at age 44 compared to the median age at diagnosis of 55 years.[3] At presentation, most patients have splenomegaly and mono- or pancytopenia, with few circulating neoplastic cells, and the disease usually follows an indolent clinical course. In contrast, this patient had leukocytosis with severe neutropenia, anemia, and thrombocytopenia as well as complications of these cytopenias, including subdural hematoma after minimal trauma, severe bleeding requiring intubation for airway protection, and sepsis due to MSSA bacteremia.

The mucosal lymphocyte antigen CD103 is a sensitive marker, and when co-expressed with pan B-cell markers is highly suggestive of HCL. However, this patient also had leukocytosis and lymphocytosis, which are more common in HCL variant (HCL-v).[6] The positive CD25 expression by flow cytometry, uniform annexin A1 staining on the bone marrow specimen *(Figure 1d)*, and presence of the *BRAF* p.V600E mutation excluded the diagnosis of HCL-v.[7–9] This patient's dramatic response to cladribine is typical of HCL.[10]

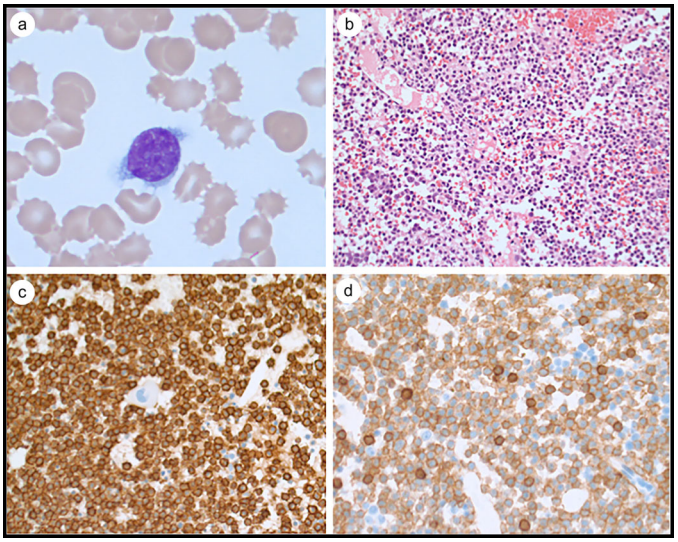

Figure 1. Representative images of lymphocytes from peripheral blood film and bone marrow core biopsy. Complete blood count at presentation demonstrated severe macrocytic anemia with anisopoikilocytosis, increased polychromasia, and rare circulating nucleated red blood cells; marked thrombocytopenia; and moderate leukocytosis (25 K/μL) with absolute lymphocytosis. **(a)** Most lymphocytes were medium-sized with coarse chromatin and moderately abundant pale basophilic cytoplasm showing distinctive circumferential "hairy" projections. **(b)** Hematoxylin and eosin (H&E)–stained sections revealed a hypercellular bone marrow for age (>95% cellularity) with extensive involvement by B-cell lymphoma. 200× magnification. The neoplastic B cells were positive for **(c)** CD20 and **(d)** annexin-A1, consistent with a diagnosis of hairy cell leukemia.

HCL should be suspected in all patients with pancytopenia and splenomegaly. It is a curable disease that is uniquely sensitive to nucleosides (purine analogs) such as pentostatin and cladribine, and delay in diagnosis due to abnormal presentation of the disease could lead to mortality that may otherwise have been prevented.

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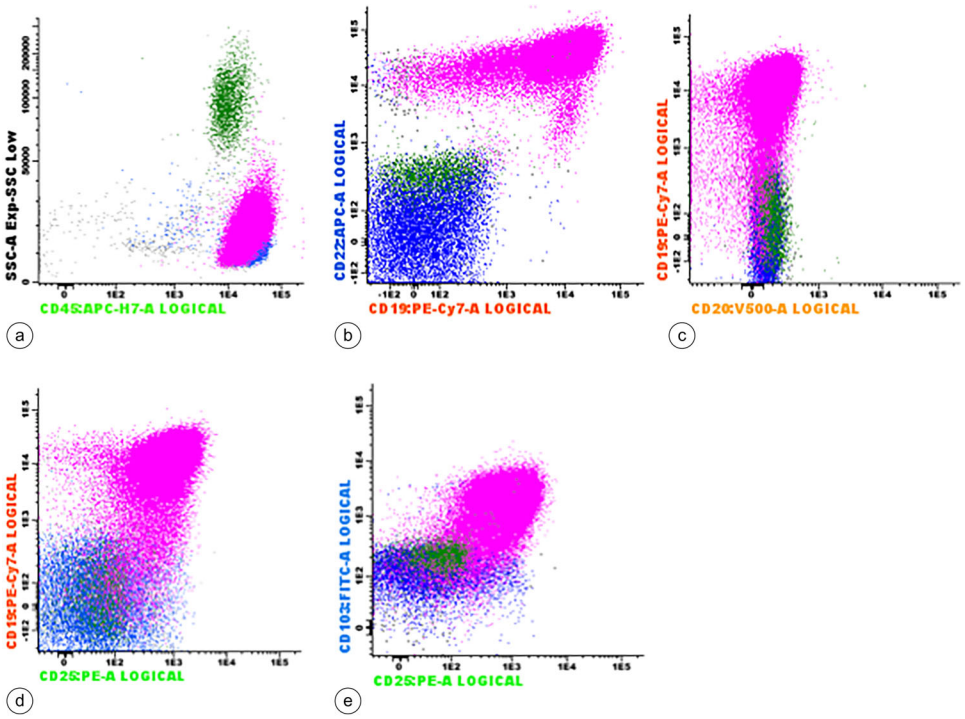

Figure 2. Flow cytometry immunophenotype of peripheral blood at diagnosis, selected histograms. Flow cytometry was performed on a peripheral blood sample. The immunophenotypic profile of the **(a)** CD45 bright neoplastic B cells (pink) consists of bright co-expression of **(b)** CD19 and CD22, **(c)** dimmer CD20, and expression of **(d)** CD25 and **(e)** CD103. The cells also expressed CD23, CD200, and FMC7 and were negative for CD5 and CD10. This population comprised approximately 80% of total events. Granulocytes, green; non-neoplastic lymphocytes, blue.

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